Published in final edited form as:

Curr Opin Neurobiol. 2013 June ; 23(3): 381–386. doi:10.1016/j.conb.2013.01.008.

PHYSIOLOGICAL BASIS FOR EMOTIONAL MODULATION OF MEMORY CIRCUITS BY THE AMYGDALA

Rony Paz¹ and Denis Pare²

¹Department of Neurobiology, Weizmann Institute of Science, Rehovot 76100, Israel

²Center for Molecular & Behavioral Neuroscience, Rutgers State University, Newark, NJ 07102, USA

Abstract

Classical experiments have demonstrated that the amygdala facilitates synaptic plasticity in other brain structures (e.g. hippocampus, basal ganglia) believed to constitute the storage sites for various types of memory. Here, we summarize new developments in our understanding of how the amygdala facilitates the formation of emotional memories. Recent insights into this question have come from studies relying on simultaneous recording of neurons in multiple brain regions during learning. This approach has revealed that in emotionally arousing conditions, whether positively or negatively valenced, the amygdala allows incoming information to be processed more efficiently in distributed cerebral networks. This review also highlights the need to understand how different brain regions act in parallel to efficiently achieve one goal.

Keywords

amygdala; emotion; learning; memory

Support for the notion that emotional arousal generally improves memory comes from introspective reports and controlled laboratory studies[1,2]. From an evolutionary perspective, given the brain's limited capacity for storage and recall, the usefulness of facilitating memory for experiences that evoke strong emotions, either positive or negative[3], is obvious[4•]. This phenomenon manifests itself in several ways: (a) a shorter learning period, meaning that only one or few occurrences of the experience are required to form a lasting memory[5]; (b) an increased reliability, whereby an emotionally-arousing experience is more likely to be remembered than a neutral one[1,6•,7]; (c) a more faithful transfer to long-term stores (consolidation) [8,9•]; and (d) an increased resistance to future perturbations. These four features of an emotional memory have one point in common: they require reliable and efficient encoding of the initial experience.

One way in which the brain can achieve this goal is to rely on dedicated anatomical pathways. This is the case for classical tone-shock fear-conditioning where the input and output pathways have been thoroughly delineated and studied[10,11•,12•]. However, for

© 2013 Elsevier Ltd. All rights reserved

Correspondence: Rony Paz Dept. of Neurobiology, Weizmann Institute of Science 1 Herzl st. Rehovot 76100, Israel rony.paz@weizmann.ac.il Denis Pare Center for Molecular & Behavioral Neuroscience 197 university avenue, Newark, NJ 7102, USA pare@andromeda.rutgers.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

more complex memories, the existence of such dedicated pathways is debated[13]. In general, the direct pathway solution, while very efficient for specific tasks, is hard to implement for all possible input domains. Hence, the complexity of real life experiences and the flexibility they require pose a challenge to brain circuitry.

An alternative to the dedicated circuit model is to modulate the efficacy of existing pathways when stimuli or the contexts have an emotional tag. In this scenario, the same pathways are used to encode and store 'neutral' and emotional memories, but they are modulated to act more efficiently when there is an emotional context, or when the stimulus itself has valence. Many studies have pointed to the amygdala as a major contributor to this process. These range from analyses of memory deficits in amygdala-lesioned patients[7], functional imaging experiments that revealed heightened amygdala activity during emotional encoding[14,15], as well as pharmacological studies in rats showing that amygdala activity during and/or shortly after learning is required for the facilitation of memory by emotions[16].

Crucially, the amygdala is in an ideal anatomical position to perform this task[17–19]. Indeed, it sends direct projections that can modulate two major learning and memory systems: the medial temporal lobe[20], and striatum[21]. Moreover, the amygdala projects to modulatory systems of the basal forebrain and brainstem that regulate the excitability of the entire telencephalon[20]. Hence, the amygdala is well positioned to regulate the processing of incoming information when it is important for survival. This is true in rodents and felines, but even more so in primates, where the cortical projections of the amygdala are much more extensive[22]. While previous studies have established that the amygdala is strongly recruited in conditions of emotional arousal, whether the valence is positive or negative, delineating how exactly the amygdala modulates different memory systems requires parallel electrophysiological recordings from the amygdala and its targets. Recently, such investigations were carried out, yielding important novel insights.

Modulation of information transfer in the rhinal cortices by the amygdala

The rhinal cortices occupy a strategic position in the temporal lobe because they relay most neocortical sensory inputs to the hippocampus and they constitute the main return path for hippocampal outputs to the neocortex[23]. Although their precise role in memory is still debated[24,25], it is clear that the rhinal cortices are not mere relay stations. Indeed, rhinal neurons exhibit different patterns of memory-related activity compared to hippocampal cells[25], such as familiarity/novelty effects and stimulus selective delay firing in delayed-matching-to-sample tasks. Consistent with this, lesion studies in rodents and primates indicate that the rhinal cortices are critical for recognition and associative memory[26]. Thus, it appears that the rhinal cortices play two complementary roles in memory. First, they constitute a memory system by themselves. Second, they serve as the main interface between associative neocortical areas and the hippocampus.

In broad strokes, the rhinal cortices can be described as being comprised of (a) an input station (perirhinal and postrhinal cortices; hereafter collectively referred to as PRC) that receives sensory information from associative neocortical areas, and (b) an output stage (the lateral and medial entorhinal regions) that forms reciprocal connections with the hippocampus and PRC[27]. Although these different rhinal regions are strongly interconnected, physiological experiments in cats and guinea pigs have revealed that PRC transfer of neocortical inputs to the entorhinal cortex (and in the opposite direction) occurs with a very low probability[28–30]. Consistent with this, connections between these various regions not only involve glutamatergic neurons, but also a very large contingent of inhibitory connections[31,32]. As a result, the rhinal cortices constitute an inhibitory gating

mechanism that regulates interactions between associative neocortical areas and the hippocampus[27]. In principle, this gating design should allow for more or less efficient information crossover, based on need. A good candidate to regulate this gating mechanism is the amygdala. Indeed, the basolateral amygdala (BLA) strongly projects to the perirhinal and entorhinal cortices[20], with BLA axons exclusively forming glutamatergic synapses, mostly onto principal cells[33]. Hence, the amygdala is ideally positioned to modulate information transfer through the perirhinal and entorhinal cortices, by exciting neurons in both regions, either concomitantly or consecutively.

This possibility was tested by recording triplets of perirhinal, entorhinal, and BLA neurons (Fig. 1A1) while cats learned an appetitive trace conditioning task, where a visual conditioned stimulus (CS) predicted delivery of a liquid reward, after a delay[34••]. The use of trace conditioning is significant here because this type of learning depends on the hippocampus[35]. Correlative analyses of spontaneous perirhinal and entorhinal firing confirmed that by default, the rhinal cortices indeed form a gated circuit. That is, little evidence of correlated firing was seen between perirhinal and entorhinal neurons (Fig. 1A2). However, when perirhinal-entorhinal correlations were conditioned on BLA activity, the proportion of significant correlations increased dramatically (Fig. 1A3, B). This indicates that while the rhinal cortices form a gated circuit, this gate can be lowered when BLA neurons are active. Stated otherwise, amygdala activity increases the chance that neuronal discharges in one rhinal region will fire neurons in the other. Early in learning, this effect was evident following reward delivery (Fig. 1C1). However, as the cats learned the predictive relationship between the CS and reward, this effect diminished and became locked to the CS (Fig. 1C2). This shift is reminiscent of, and might indeed be driven by, the activity of dopaminergic neurons[36].

A critical question for memory encoding and retrieval is whether BLA activity facilitates impulse transmission from perirhinal to entorhinal neurons or in the opposite direction. The design of the analyses allowed this point to be determined, revealing a preferential perirhinal to entorhinal facilitation[34]. Therefore, these findings suggest that during encoding, BLA activity facilitates rhinal transfer of neocortical activity to the hippocampus. Moreover, it was shown that increased synchrony of BLA firing at the gamma frequency (~35–45Hz) was responsible for the facilitated rhinal interactions[37]. Indeed, these fast oscillations increased in power and coherence as learning progressed, entraining spiking in the three regions.

Modulation of corticostriatal plasticity by the amygdala

In addition to motor control, the striatum plays an important role in various types of learning such as habit formation and goal-directed behavior[38,39]. The striatum receives inputs from low- and high-order cortical areas[40] and activity-dependent plasticity at these inputs is thought to underlie striatal contributions to learning[41]. In keeping with this, corticostriatal inputs can undergo NMDA-dependent long-term potentiation (LTP) *in vitro*[42]. Moreover, intra-striatal infusions of NMDA receptor antagonists interfere with the acquisition of striatal-dependent tasks in rats[43,44].

In rats, it was shown that the amygdala could also facilitate striatal-dependent memories. Local infusions of drugs that enhanced or reduced BLA activity immediately after training on striatal-dependent tasks respectively improved or impaired recall tested days later[16]. In contrast, the same manipulations performed just before testing recall had no effect[45], indicating that the BLA does not store these memories but that it facilitates storage in the striatum[46].

How does the amygdala facilitate striatal-dependent learning? Inputs from different cortical regions are processed in distinct striatal territories, and then relayed via the globus pallidus to the thalamus and from there back to the cortex[47]. Thus, the concept developed above for the rhinal cortices might apply here: the amygdala would allow improved processing of cortical inputs at the striatal level and enhance their propagation and further downstream processing. Consistent with this, the BLA sends glutamatergic projections to the ventral striatum and these contact principal (medium spiny – MSN) striatal neurons[21].

Support for this notion comes from recent in vitro studies that examined the impact of BLA inputs on corticostriatal LTP in guinea pigs. A first study revealed that BLA stimulation strongly facilitates LTP induction at cortical inputs onto MSNs[48] (Fig. 2A). This facilitation was dependent on NMDA-receptor activation at BLA synapses and it occurred even when BLA and cortical stimuli were 0.5 s apart during LTP induction. The latter observation indicated that the facilitation of corticostriatal plasticity by BLA inputs did not depend on an increased depolarization of MSNs but on other properties of BLA synapses. A follow-up study [49] revealed that these properties were (a) a higher contribution of NMDA receptors at BLA than cortical synapses and (b) the ability of BLA inputs to trigger Ca^{2+} -induced Ca^{2+} release (CICR). The latter property likely explains why BLA stimuli can facilitate corticostriatal LTP, even when BLA and cortical shocks are applied asynchronously. The lax temporal requirement for the BLA facilitation of corticostriatal plasticity seems well adapted to mediate the sustained influence of emotional arousal on learning. Finally, reminiscent of the findings obtained in the rhinal cortices[37], it was found in cats that gamma oscillations coordinate neuronal interactions between the amygdala and striatum in a learning-dependent manner[50] (Fig. 2B). Therefore, it is possible that gamma is a general mechanism used by the amygdala to mediate its influence on target structures.

Conclusion

The amygdala is well positioned to modulate information transfer in different circuits of the brain. In this review, we presented evidence that two major memory circuits are indeed modulated by the amygdala in emotionally arousing conditions. For some simple types of learning, particularly those related to fear, dedicated pathways have evolved to allow fast formation of stimulus associations. However, given the richness of daily-life and the flexibility it requires, memory cannot depend on the formation of a 'labeled-line' for each possible input-output combination. A computationally economical solution to this problem is to create a system that allows emotional/motivational information to modulate other, already existing pathways to achieve faster and more efficient encoding of relevant stimulus contingencies. For clarity, we focused here on striatal- and hippocampal-dependent memories, yet similar evidence recently emerged for the importance of the monkey prefrontal cortex in such interactions[51•,52•,53,54]. Importantly, to find mechanistic evidence of these modulation, one must record several neurons in several brain regions simultaneously, and develop tools to analyze the complex conditional computations that take place in distributed networks[55].

Several questions still remain: how does the system decide which information should be prioritized? What is the relationship between learned emotional information and innate tendencies? What makes emotional memory, following the initial efficient encoding, more resistant to subsequent perturbations? There is ample evidence that the amygdala is involved in these phenomena as well. A major challenge for future studies will be elucidate the underlying mechanisms.

Acknowledgments

This work was supported by NIMH grant MH-073610 to D.P.; and ERC-FP7-StG grant #281171 to R.P.

References and recommended reading

1. Cahill L, McGaugh JL. Mechanisms of emotional arousal and lasting declarative memory. *Trends Neurosci.* 1998; 21:294–299. [PubMed: 9683321]
2. Christianson, SA. *Handbook of Emotion and Memory: Current Research and Theory.* Erlbaum, Hillsdale; 1992.
3. Hamann SB, Cahill L, Squire LR. Emotional perception and memory in amnesia. *Neuropsychology.* 1997; 11:104–113. [PubMed: 9055274]
4. Roozendaal B, McGaugh JL. Memory modulation. *Behav Neurosci.* 2011; 125:797–824. [PubMed: 22122145] • This comprehensive review provides a summary of studies documenting the pervasive influence of emotional arousal on different aspects of memory, including encoding, consolidation, recall, and extinction.s
5. Fanselow MS, Poulos AM. The neuroscience of mammalian associative learning. *Annu Rev Psychol.* 2005; 56:207–234. [PubMed: 15709934]
6. Dirnberger G, Hesselmann G, Roiser JP, Preminger S, Jahanshahi M, Paz R. Give it time: Neural evidence for distorted time perception and enhanced memory encoding in emotional situations. *Neuroimage.* 2012; 63:591–599. [PubMed: 22750720] • This elegant study combines functional imaging and psychophysics in humans to study the mechanisms of distorted time perception and enhanced memory formation seen in emotionally arousing conditions.
7. Adolphs R, Tranel D, Buchanan TW. Amygdala damage impairs emotional memory for gist but not details of complex stimuli. *Nat Neurosci.* 2005; 8:512–518. [PubMed: 15735643]
8. McGaugh JL. The amygdala modulates the consolidation of memories of emotionally arousing experiences. *Annu Rev Neurosci.* 2004; 27:1–28. [PubMed: 15217324]
9. Dudai Y. The restless engram: consolidations never end. *Annu Rev Neurosci.* 2012; 35:227–247. [PubMed: 22443508] • This insightful paper reviews the most recent advances in our understanding of the continued process of memory consolidation.
10. Pape HC, Pare D. Plastic synaptic networks of the amygdala for the acquisition, expression, and extinction of conditioned fear. *Physiol Rev.* 2010; 90:419–463. [PubMed: 20393190]
11. Johansen JP, Cain CK, Ostroff LE, LeDoux JE. Molecular mechanisms of fear learning and memory. *Cell.* 2011; 147:509–524. [PubMed: 22036561] • This review offers a comprehensive analysis of the multiple intracellular signaling pathways that underlie fear-conditioning related plasticity in the lateral amygdala.
12. Pare D, Duvarci S. Amygdala microcircuits mediating fear expression and extinction. *Curr Opin Neurobiol.* 2012; 22:717–723. [PubMed: 22424846] • This review summarizes the latest developments in our understanding of amygdala networks that support classical fear conditioning. These advances indicate that fear learning depends on more complex networks than initially believed, including coordinated interactions between multiple excitatory and inhibitory circuits within the amygdala.
13. Pessoa L, Adolphs R. Emotion processing and the amygdala: from a 'low road' to 'many roads' of evaluating biological significance. *Nat Rev Neurosci.* 2010; 11:773–783. [PubMed: 20959860]
14. Cahill L, Haier RJ, Fallon J, Alkire MT, Tang C, Keator D, Wu J, McGaugh JL. Amygdala activity at encoding correlated with long-term, free recall of emotional information. *Proc Natl Acad Sci U S A.* 1996; 93:8016–8021. [PubMed: 8755595]
15. Nili U, Goldberg H, Weizman A, Dudai Y. Fear thou not: activity of frontal and temporal circuits in moments of real-life courage. *Neuron.* 2010; 66:949–962. [PubMed: 20620879]
16. Packard MG, Cahill L, McGaugh JL. Amygdala modulation of hippocampal-dependent and caudate nucleus-dependent memory processes. *Proc Natl Acad Sci U S A.* 1994; 91:8477–8481. [PubMed: 8078906]
17. McDonald AJ. Cortical pathways to the mammalian amygdala. *Prog Neurobiol.* 1998; 55:257–332. [PubMed: 9643556]

18. Amaral DG, Price JL. Amygdalo-cortical projections in the monkey (*Macaca fascicularis*). *J Comp Neurol*. 1984; 230:465–496. [PubMed: 6520247]
19. Barbas H, Zikopoulos B, Timbie C. Sensory pathways and emotional context for action in primate prefrontal cortex. *Biol Psychiatry*. 2011; 69:1133–1139. [PubMed: 20889144] • This review places amygdalo-prefrontal interactions within the larger context of prefrontal connectivity, thereby offering a theoretical framework for the modulation of prefrontal operations by emotional contexts.
20. Pitkanen, A. Connectivity of the rat amygdaloid complex. In: Aggleton, JP., editor. *The Amygdala*. Oxford university press; 2000.
21. Kita H, Kitai ST. Amygdaloid projections to the frontal cortex and the striatum in the rat. *J Comp Neurol*. 1990; 298:40–49. [PubMed: 1698828]
22. Young MP, Scannell JW, Burns GA, Blakemore C. Analysis of connectivity: neural systems in the cerebral cortex. *Rev Neurosci*. 1994; 5:227–250. [PubMed: 7889215]
23. Witter, MP.; Wouterlood, F. *The parahippocampal region*. oxford university press; Oxford: 2002.
24. Squire LR, Wixted JT. The cognitive neuroscience of human memory since H.M. *Annu Rev Neurosci*. 2011; 34:259–288. [PubMed: 21456960] • This authoritative review paper considers how different structures of the medial temporal lobe contribute to various forms of memories.
25. Suzuki WA. Untangling memory from perception in the medial temporal lobe. *Trends Cogn Sci*. 2010; 14:195–200. [PubMed: 20227327]
26. Brown MW, Aggleton JP. Recognition memory: what are the roles of the perirhinal cortex and hippocampus? *Nat Rev Neurosci*. 2001; 2:51–61. [PubMed: 11253359]
27. de Curtis M, Pare D. The rhinal cortices: a wall of inhibition between the neocortex and the hippocampus. *Prog Neurobiol*. 2004; 74:101–110. [PubMed: 15518955]
28. Biella G, Uva L, de Curtis M. Network activity evoked by neocortical stimulation in area 36 of the guinea pig perirhinal cortex. *J Neurophysiol*. 2001; 86:164–172. [PubMed: 11431498]
29. Pelletier JG, Apergis J, Pare D. Low-probability transmission of neocortical and entorhinal impulses through the perirhinal cortex. *J Neurophysiol*. 2004; 91:2079–2089. [PubMed: 15069098]
30. Logothetis NK, Eschenko O, Murayama Y, Augath M, Steudel T, Evrard HC, Besserve M, Oeltermann A. Hippocampal-cortical interaction during periods of subcortical silence. *Nature*. 2012; 491:547–553. [PubMed: 23172213] • Combining functional imaging and field potential recordings in monkeys, this paper shows that hippocampal sharp-wave ripples are associated with widespread cortical activation and subcortical inhibition. However, strong electrical stimulation of the entorhinal cortex, the main hippocampal output, failed to cause significant cortical activations. This suggests that ripple activity coincides with, but does not cause, these widespread and region-specific changes in cerebral activity.
31. Pinto A, Fuentes C, Pare D. Feedforward inhibition regulates perirhinal transmission of neocortical inputs to the entorhinal cortex: ultrastructural study in guinea pigs. *J Comp Neurol*. 2006; 495:722–734. [PubMed: 16506192]
32. Unal G, Pare JF, Smith Y, Pare D. Differential connectivity of short- vs. long-range extrinsic and intrinsic cortical inputs to perirhinal neurons. *J Comp Neurol*. In Press.
33. Smith Y, Pare D. Intra-amygdaloid projections of the lateral nucleus in the cat: PHA-L anterograde labeling combined with postembedding GABA and glutamate immunocytochemistry. *J Comp Neurol*. 1994; 342:232–248. [PubMed: 7911130]
34. Paz R, Pelletier JG, Bauer EP, Pare D. Emotional enhancement of memory via amygdala-driven facilitation of rhinal interactions. *Nat Neurosci*. 2006; 9:1321–1329. [PubMed: 16964249] • Recording simultaneously in three different brain regions of the cat (the amygdala, the perirhinal, and the entorhinal cortex) and using a novel analysis technique, this study showed that the amygdala facilitates transfer of information between the rhinal cortices during acquisition of novel reward associations.
35. Shors TJ. Memory traces of trace memories: neurogenesis, synaptogenesis and awareness. *Trends Neurosci*. 2004; 27:250–256. [PubMed: 15111006]
36. Schultz W. Dopamine signals for reward value and risk: basic and recent data. *Behav Brain Funct*. 2010; 6:24. [PubMed: 20416052]

37. Bauer EP, Paz R, Pare D. Gamma oscillations coordinate amygdalo-rhinal interactions during learning. *J Neurosci.* 2007; 27:9369–9379. [PubMed: 17728450]
38. Packard MG, Knowlton BJ. Learning and memory functions of the Basal Ganglia. *Annu Rev Neurosci.* 2002; 25:563–593. [PubMed: 12052921]
39. Pennartz CM, Berke JD, Graybiel AM, Ito R, Lansink CS, van der Meer M, Redish AD, Smith KS, Voorn P. Corticostriatal Interactions during Learning, Memory Processing, and Decision Making. *J Neurosci.* 2009; 29:12831–12838. [PubMed: 19828796]
40. Wilson, CJ. Basal ganglia. In: Shepherd, GM., editor. *The synaptic organization of the brain.* Oxford university press; 1998.
41. Lovinger DM. Neurotransmitter roles in synaptic modulation, plasticity and learning in the dorsal striatum. *Neuropharmacology.* 2010; 58:951–961. [PubMed: 20096294]
42. Calabresi P, Maj R, Pisani A, Mercuri NB, Bernardi G. Long-term synaptic depression in the striatum: physiological and pharmacological characterization. *J Neurosci.* 1992; 12:4224–4233. [PubMed: 1359031]
43. Packard MG, Teather LA. Posttraining injections of MK-801 produce a time-dependent impairment of memory in two water maze tasks. *Neurobiol Learn Mem.* 1997; 68:42–50. [PubMed: 9195588]
44. Packard MG, Teather LA. Double dissociation of hippocampal and dorsal-striatal memory systems by posttraining intracerebral injections of 2-amino-5-phosphonopentanoic acid. *Behav Neurosci.* 1997; 111:543–551. [PubMed: 9189269]
45. Packard MG, Teather LA. Amygdala modulation of multiple memory systems: hippocampus and caudate-putamen. *Neurobiol Learn Mem.* 1998; 69:163–203. [PubMed: 9619995]
46. Packard MG, Cahill L. Affective modulation of multiple memory systems. *Curr Opin Neurobiol.* 2001; 11:752–756. [PubMed: 11741029]
47. Morris G, Schmidt R, Bergman H. Striatal action-learning based on dopamine concentration. *Exp Brain Res.* 2010; 200:307–317. [PubMed: 19904530]
48. Popescu AT, Saghyan AA, Pare D. NMDA-dependent facilitation of corticostriatal plasticity by the amygdala. *Proc Natl Acad Sci U S A.* 2007; 104:341–346. [PubMed: 17182737]
49. Popescu AT, Saghyan AA, Nagy FZ, Pare D. Facilitation of corticostriatal plasticity by the amygdala requires Ca²⁺-induced Ca²⁺ release in the ventral striatum. *J Neurophysiol.* 2010; 104:1673–1680. [PubMed: 20554836]
50. Popescu AT, Popa D, Pare D. Coherent gamma oscillations couple the amygdala and striatum during learning. *Nat Neurosci.* 2009; 12:801–807. [PubMed: 19430471]
51. Livneh U, Paz R. Amygdala-prefrontal synchronization underlies resistance to extinction of aversive memories. *Neuron.* 2012; 75:133–142. [PubMed: 22794267] •• This study analyzes the mechanisms that determine the resistance of aversive memories to extinction. It relied on simultaneous recordings of dACC and amygdala neurons in macaque monkeys undergoing fear conditioning with continuous or partial reinforcement schedules. This revealed that the strength of dACC-amygdala correlations during conditioning predicted later resistance of aversive memories to extinction.
52. Klavir O, Genud-Gabai R, Paz R. Low-frequency stimulation depresses the primate anterior-cingulate-cortex and prevents spontaneous recovery of aversive memories. *J Neurosci.* 2012; 32:8589–8597. [PubMed: 22723700] • This study combines microstimulation and unit recordings in the dorsal anterior cingulate cortex (dACC) of macaque monkeys to show that reducing dACC excitability during extinction training prevents spontaneous recovery of fear memories.
53. Paz R, Bauer EP, Pare D. Theta synchronizes the activity of medial prefrontal neurons during learning. *Learn Mem.* 2008; 15:524–531. [PubMed: 18612069]
54. Paz R, Bauer EP, Pare D. Learning-related facilitation of rhinal interactions by medial prefrontal inputs. *J Neurosci.* 2007; 27:6542–6551. [PubMed: 17567815]
55. Paz R, Bauer EP, Pare D. Measuring correlations and interactions among four simultaneously recorded brain regions during learning. *J Neurophysiol.* 2009; 101:2507–2515. [PubMed: 19244352]

The rhinal cortices gate information transfer between the neocortex and hippocampus.

The amygdala enhances neocortical-hippocampal interactions via the rhinal cortices.

The amygdala facilitates induction of plasticity at corticostriatal synapses.

The amygdala uses gamma oscillations to influence its targets.

Figure 1.

BLA facilitation of rhinal interactions. (**A1**) Ventral view of cat brain showing position of microelectrodes in the amygdala, and rhinal cortices. Cross indicates orientation (M, medial; L, lateral; R, rostral; C, caudal). **Abbreviations:** BLA, basolateral amygdala, EC, entorhinal cortex; rh, rhinal sulcus. (**A2–3**) Cross-correlogram of entorhinal firing around perirhinal spikes. No correlation is seen when all spikes are considered (**A2**). In contrast, a strong correlation is seen when the analysis is restricted to perirhinal spikes that occurred within ± 30 ms of BLA spikes (**A3**). (**B1**) Spike-triggered-joint-histogram (STJH) plotting relative timing of entorhinal (y-axis) and perirhinal (x-axis) firing around BLA spikes. (**B2**) The proportion of significant STJHs (y-axis) increases after delivery of unexpected rewards (time 0 in x-axis). (**C**) Proportion of significant STJHs (y-axis) during trace-conditioning trials (x-axis) at early (**C1**) and late (**C2**) stages of training.

Figure 2.

Facilitation of striatal plasticity by BLA inputs. (**A1**) In medium spiny neurons of the striatum, pairing electrical stimulation of BLA and cortical (C) inputs causes a persistent (x-axis) potentiation of corticostriatal inputs (EPSP slope, y-axis, **A1**), much more so than seen after pairing two cortical sites (**A2**). (**B**) Learning-dependent fluctuations in amygdalo-striatal gamma coherence during appetitive stimulus-response task. Over a period of 5 days, cats learned that one of two auditory stimuli (CS⁺, T1) predicted reward delivery at CS⁺ offset, whereas a second tone (CS⁻, T2) did not. Then, reward contingencies were reversed. (**B1**) Amygdalo-striatal gamma coherence (T1-T2) as a function of time (x-axis). Gray shading indicates reversal period. Examples of time-dependent fluctuations in amygdalo-striatal gamma coherence at the end of the initial training period (Day 5, **B2**) and after reversal of the reinforcement contingencies (r3, **B3**).